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**Citation for published version:**

Gale, CR, Martyn, CN & Cooper, C 1996, 'Cognitive impairment and mortality in a cohort of elderly people', *British Medical Journal (BMJ)*, vol. 312, no. 7031, pp. 608-611. <https://doi.org/10.1136/bmj.312.7031.608>

**Digital Object Identifier (DOI):**

[10.1136/bmj.312.7031.608](https://doi.org/10.1136/bmj.312.7031.608)

**Link:**

[Link to publication record in Edinburgh Research Explorer](#)

**Published In:**

British Medical Journal (BMJ)

**Publisher Rights Statement:**

© Gale, C. R., Martyn, C. N., & Cooper, C. (1996). Cognitive impairment and mortality in a cohort of elderly people. *BMJ*, 312(7031), 608-611 doi: 10.1136/bmj.312.7031.608

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## Paper

# Cognitive impairment and mortality in a cohort of elderly people

*BMJ* 1996; 312 doi: <http://dx.doi.org/10.1136/bmj.312.7031.608> (Published 9 March 1996)

Cite this as: *BMJ* 1996;312:608

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Accepted 1 November 1995

## Abstract

**Objectives:** To investigate the relation between cognitive function and cause specific mortality in people aged 65 and over.

**Design:** A 20 year follow up study of a cohort of randomly selected elderly people

living in the community who in 1973-4 had taken part in a nutritional survey funded by the Department of Health and Social Security.

**Setting:** Eight areas in Britain (five in England, two in Scotland, and one in Wales).

**Subjects:** 921 men and women whose cognitive function was assessed by a geriatrician in 1973-4 and for whom data on health, socioeconomic circumstances, and diet had been recorded.

**Results:** Cognitive impairment was associated with increased mortality, in particular death from ischaemic stroke. Those who scored 7 or less on the Hodkinson mental test had a relative risk of dying from stroke of 2.8 (95% confidence interval 1.4 to 5.5), compared with those who gained the maximum score (10), after adjustment for age, sex, blood pressure, serum cholesterol concentration, and vitamin C intake. These associations were independent of illness or social class. At the time of the nutritional survey, cognitive function was poorest in those with the lowest vitamin C status, whether measured by dietary intake or plasma ascorbic acid concentration. The relation between vitamin C status and cognitive function was independent of age, illness, social class, or other dietary variables.

**Conclusion:** The relation between cognitive function and risk of death from stroke suggests that cerebrovascular disease is an important cause of declining cognitive function. Vitamin C status may be a determinant of cognitive function in elderly people through its effect on atherogenesis. A high vitamin C intake may protect against both cognitive impairment and cerebrovascular disease.

## Key messages

- Key messages
- In this prospective study of 921 elderly people cognitive impairment was a strong predictor of death from ischaemic stroke
- Low vitamin C intake and low plasma ascorbate concentrations were also important risk factors for death from stroke
- Cognitive performance was poorest in people with the lowest vitamin C status
- A high vitamin C intake may protect against both cognitive impairment and

## cerebrovascular disease

### Introduction

Poor cognitive performance has been associated with increased mortality in several studies of elderly people, but the underlying mechanisms remain unclear.<sup>1 2 3</sup>

Evidence exists linking high levels of risk factors for cerebrovascular disease with poorer performance in various cognitive tasks,<sup>4 5</sup> and the results of a recent population based study from the Netherlands showed that elderly people with atherosclerotic disease of the carotid arteries were more likely to be cognitively impaired.<sup>6</sup> To investigate further the relation between cognitive impairment and cardiovascular disease we examined performance on a simple test of cognitive function and cause specific mortality in a 20 year follow up study of a national sample of elderly people who had taken part in a survey in 1973-4.

The Department of Health and Social Security had carried out this survey using random samples of elderly people across Britain to assess the nutritional state of the elderly population. The areas were chosen so that the socioeconomic characteristics of the study sample were representative of elderly people in Britain who were not living in an institution. As part of this study, subjects were assessed by a geriatrician who tested their mental status.

### Subjects and methods

During 1973 and 1974, 1775 people in eight areas of Britain (five in England, two in Scotland, and one in Wales) were randomly sampled from family practitioner committees' lists of all patients aged 65 years and over. The areas were Islington, Harrow, Hastings, Bristol, Salford, Rutherglen, Angus, and Merthyr Tydfil. Stratified sampling was used to obtain equal numbers of men and women aged 65 to 74 and 75 and over.

Of the subjects selected, 1688 were living at home and were asked to take part in the study; 1419 (720 men, 699 women; 84%) of these agreed. In all, 983 (69%) of those who participated agreed to be examined by a geriatrician.

Participants kept a diary of every item of food or drink consumed over a week. They were given a set of scales to weigh each item. An interviewer visited them at least four times and administered a questionnaire on their socioeconomic circumstances.

If the participants could not cope with the weighing procedure, the interviewer used the food diary to quantify their consumption; food purchases were used as a cross check. Nutrient intake was calculated with a food composition table compiled by the Department of Health and Social Security.

The geriatricians measured height, weight, and blood pressure and recorded current smoking habits and drug treatment in the past six months. A sample of blood was taken for biochemical analysis. Cognitive performance was measured with the Hodkinson abbreviated mental test.<sup>7</sup> Ten people were excluded from this part of the examination owing to severe deafness, dysphasia, or language difficulties.

Of the 973 subjects whose cognitive function was assessed, all except 10 had usable dietary records. We traced 921 (95%) of these subjects through the NHS central register. We obtained death certificates for those who had died and coded all causes of death entered in parts I and II according to ICD-9 (international classification of diseases, ninth revision). All cases where coronary heart disease (codes 410-414), ischaemic stroke, excluding subarachnoid and intracerebral haemorrhage (codes 433-438), cancer (codes 140-208), or respiratory disease (codes 460-519) was mentioned on the death certificate were counted as deaths from these causes.

To identify potential confounders of the relation between cognitive function and subsequent mortality we examined the associations between score on the Hodkinson mental test and baseline measures of social class, health, and diet using logistic regression. We divided the subjects into two groups according to their score on the Hodkinson test: (a) those who scored the maximum of 10 (no cognitive impairment) and (b) those with a score of 9 or less (some cognitive impairment). The frequency distributions of all the dietary intake variables and plasma ascorbic acid concentrations were skewed, and we used logarithmic transformations when analysing these as continuous variables. The results are shown as odds ratios within thirds of the distribution of the variables, except for age and social class.

A Cox's proportional hazard model was used to examine the associations between cognitive function and mortality. The subjects were divided into three groups according to their score on the Hodkinson test: (a) those who scored 10, (b) those who scored 8 or 9 (slight cognitive impairment), and (c) those who scored 7 or less (more severe impairment). Risk estimates were adjusted for sex and for age in five

year strata; because of small numbers a 10 year stratum was used for the oldest age group. The results are shown as relative risks (hazard ratios) within thirds of the distribution of the variables, except for cognitive function and cardiovascular disease.

## Results

In both men and women the proportion showing evidence of cognitive impairment on the Hodkinson test increased significantly with age, though even in the older age groups a large percentage gained the maximum score (table 1). No significant differences in cognitive function were found between the sexes.

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Table 1

Distribution of scores on Hodkinson mental test by age and sex. Values are numbers (percentages) of subjects

Lower scores on the Hodkinson test were more common in people from manual classes and in those with higher diastolic blood pressure. We found no relation between cognitive function and systolic blood pressure, current smoking status, general state of physical health, or recorded diagnosis of cancer (n=22), chronic respiratory disease (n=133), diabetes (n=32), ischaemic heart disease (n=141), stroke (n=27), peripheral vascular disease (n=62), congestive cardiac failure (n=73), or depression (n=15). Of the dietary variables, vitamin C intake showed the strongest relation with cognitive function. None of the other dietary intake variables was significantly associated with risk of cognitive impairment independently of vitamin C intake. We found a similar relation between plasma ascorbic acid concentration and cognitive function. In multivariate analysis, after age was controlled for, vitamin C status, diastolic blood pressure, and social class remained significant independent correlates of cognitive function (table 2).

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Table 2

Odds ratios (95% confidence interval) for cognitive impairment

ALL CAUSE MORTALITY

During the 20 years of follow up 842 subjects died. All cause mortality was highest in those who had had the poorest cognitive function. Subjects who scored 7 or less on the Hodkinson mental test had a relative risk of death of 2.2 compared with those with the maximum score of 10, after adjustment for age and sex. Those with raised diastolic blood pressure and those with a recorded diagnosis of cardiovascular disease when examined in 1973-4 had significantly increased mortality. Of the dietary variables, vitamin C intake showed the strongest relation with mortality. No other dietary variable was related to mortality independently of vitamin C intake. We found no association between all cause mortality and systolic blood pressure, serum cholesterol concentration, current smoking status, body mass index, a recorded diagnosis of cancer in 1973-4, or social class.

In multivariate analysis cognitive function, diastolic blood pressure, cardiovascular disease, and vitamin C status (whether measured by dietary intake or plasma ascorbic acid concentration) remained significant predictors of mortality. Table 3 shows the relative risks of all cause mortality for these variables.

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Table 3

Relative risks (95% confidence interval) of all cause mortality according to cognitive function and other risk factors

Cognitive function and vitamin C intake might have been influenced by the presence of serious illness. We therefore repeated the analysis excluding all those who died in the first two years of follow up. Both variables remained significant predictors of earlier death.

CAUSE SPECIFIC MORTALITY

The major causes of death in this elderly cohort were coronary heart disease, stroke, cancer, and respiratory disease. Cognitive function was not associated with risk of death from coronary heart disease, cancer, or respiratory disease but was



strongly associated with risk of death from ischaemic stroke. Compared with those who gained the maximum score, those who scored 7 or less on the Hodkinson mental test had a relative risk of dying from stroke of 3.3 and those who scored 8 or 9 had a relative risk of 1.7. In a previous study of this cohort vitamin C status, blood pressure, and serum cholesterol concentration were associated with risk of death from stroke.<sup>8</sup> Even after adjustment was made for these factors and for a diagnosis of cardiovascular disease in 1973-4 with multivariate analysis, cognitive function remained a significant predictor of death from stroke. Those who had the poorest cognitive function had a relative risk of mortality from stroke of 2.8 compared with those who showed no evidence of cognitive impairment. Table 4 shows the relative risks of mortality from stroke for these variables. Similar results were obtained when systolic blood pressure was substituted in the model for diastolic blood pressure. When the analysis was repeated excluding all those who died in the first two years of follow up, all the variables shown in table 4 remained strong predictors of mortality from stroke.

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Table 4

Relative risks (95% confidence interval) of mortality from stroke according to cognitive function and other risk factors

## Discussion

In this 20 year follow up study of elderly men and women cognitive performance was a strong predictor of mortality, in particular of death from ischaemic stroke. People with the poorest cognitive function were nearly three times as likely to die from stroke as those who showed no evidence of cognitive impairment, after adjustment for age, sex, and other cardiovascular risk factors. Cognitive function was not associated with any other major cause of death. At baseline, the subjects with cognitive impairment had significantly higher diastolic blood pressure and a lower vitamin C status. Both these factors were also strong predictors of death from stroke.

One potential weakness in our results comes from the use of mortality data. As inaccuracies are known to exist in death certification, particularly of elderly people,



some cases of stroke may have been misclassified. Although non-differential misclassification tends to diminish the strength of an association, our results could be explained by a systematic bias among clinicians to certify deaths among cognitively impaired people as caused by stroke. But this seems unlikely since the commonest terminal events recorded on death certificates of demented people are bronchopneumonia, cardiac failure, and multiple pressure sores.<sup>9</sup> Furthermore, the relation between poor cognitive function and increased risk of death is also present with all cause mortality. Another possible weakness lies in the difficulties of assessing dietary intake of vitamin C. But the relations we found with diet were also present with plasma ascorbic acid concentration.

The results of this study are based on 921 subjects. This is 55% of those originally invited to participate in the Department of Health and Social Security's nutritional survey. All comparisons, however, have been made internally, so unless the relation between cognitive impairment and mortality is different in non-respondents or in those we were unable to trace, no bias will have been introduced.

The fact that we found no relation between all cause mortality and current smoking status and serum cholesterol concentration may be related to the age of our subjects. Factors that predict premature death, especially from cardiovascular disease, become less important in a population of elderly survivors. In a study of the Framingham cohort the association between serum cholesterol and all cause mortality disappeared in those aged over 50,<sup>10</sup> and in a study of 1118 elderly men no significant relations were found between all cause mortality and serum cholesterol concentration, systolic blood pressure, or smoking.<sup>3</sup>

An association between poor cognitive performance and lower vitamin C status has been reported previously. In 260 men and women aged over 60 years in the United States those with low blood concentrations of vitamin C, folic acid, riboflavin, or vitamin B12 had significantly lower scores on tests of memory and abstract thinking.<sup>11</sup> In 418 elderly men and women living at home in China, low blood concentrations of vitamin C, riboflavin, and folic acid were associated with low scores on the Hodkinson mental test.<sup>12</sup> One difficulty in interpreting these results stems from the cross sectional design of these studies. A lower vitamin C status may simply be a consequence rather than a cause of cognitive impairment.

But vitamin C may protect against declining cognitive function by its antioxidant

activity. Much cognitive impairment in elderly populations is thought to result from atherosclerotic disease.<sup>6 13</sup> Antioxidant vitamins may prevent the development of such disease because they protect low density lipoproteins from oxidation by free radicals, thus decreasing their atherogenic potential.<sup>14 15 16</sup> The Department of Health and Social Security's nutritional survey provided no information on the antioxidants vitamin E and  $\beta$  carotene, but in a previous study of this cohort we showed that intake of the antioxidant vitamin C was a strong predictor of subsequent death from stroke.<sup>8</sup> This finding, together with the known link between atherosclerosis and cognitive impairment, suggests that subclinical deficiency of vitamin C may be a determinant rather than a consequence of impaired cognitive function in elderly people.

Declining cognitive function and cerebrovascular disease are both common in old people. The results of this study tend to support the view that a considerable proportion of cognitive decline in the elderly population is vascular in origin. They also suggest that a high vitamin C intake, perhaps by an antiatherogenic mechanism, protects against both cognitive impairment and cerebrovascular disease. This may have important implications for prevention.

We thank the Department of Health for allowing us to use data from the 1973-4 Department of Health and Social Security's nutritional survey. We are grateful to David Coggon and Clive Osmond of the MRC's environmental epidemiology unit for advice and to Paul Winter for help with computing. The DHSS survey was coordinated by the late Professor A N Exton-Smith, and the biochemical analyses were carried out by Joan Stephen.

## Footnotes

- Funding Department of Health/Medical Research Council Nutritional Programme.
- Conflict of interest None.

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